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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,587	09/18/2003	Shuming Nie	50508-1100	1656

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THOMAS, KAYDEN, HORSTEMEYER & RISLEY, LLP
100 GALLERIA PARKWAY, NW
STE 1750
ATLANTA, GA 30339-5948

EXAMINER

YU, MELANIE J

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

JK

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/666,587	Applicant(s) NIE ET AL.	
	Examiner Melanie Yu	Art Unit 1641	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 28 February 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
- (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ They raise the issue of new matter (see NOTE below);
- (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

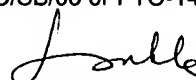
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): 35 USC 112, second paragraph rejection of claims 25-27 and 29.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
- The status of the claim(s) is (or will be) as follows:
- Claim(s) allowed: _____.
- Claim(s) objected to: _____.
- Claim(s) rejected: 1-7, 9-27, 29 and 53-96.
- Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.


LONG V. LE
 SUPERVISORY PATENT EXAMINER
 TECHNOLOGY CENTER 1600
 03/17/05

Continuation of 11. does NOT place the application in condition for allowance because: for reasons stated in the previous office action dated December 29, 2004.

Applicant's arguments against claim rejections under 35 USC 102(e) and 103(a) are not persuasive.

With respect to claims 1-7 and 9-27, Applicant argues that Chee et al. do not disclose, teach or suggest the following limitations of claim 1: "a nanospecies having a first characteristic... a porous material having the first characteristic selected from a hydrophobic characteristic, a hydrophilic characteristic, an electrostatic characteristic, and combinations thereof". However, as cited previously Chee et al. teach a hydrophobic silica (col. 3, lines 34-36) porous material (col. 7, lines 40-54) and having a plurality of pores (col. 3, lines 34-36). Chee et al. refer to microspheres (microspheres are interpreted to be nanospecies) and substrates having the same first hydrophobic, hydrophilic or electrostatic characteristics wherein the microspheres become disposed within the substrate due to the first characteristics (col. 7, lines 38-54). Chee et al. describe the substrate as being hydrophobic or hydrophilic to dispose microspheres within the substrate (col. 7, lines 38-54) and also the substrate being silica (col. 3, lines 34-36). Therefore, the substrate would be hydrophobic silica. Chee et al. disclose the nanocrystals and microspheres being disclosed in the silica (col. 7, lines 38-54; col. 34-37), and the microspheres comprising the optical signature which is a nanocrystal (col. 13, lines 36-60). Therefore, the nanocrystals and microspheres are part of the same structure and collectively comprise the first and second characteristics of being hydrophobic and optically detectable, respectively. Applicant argues that the nanocrystals are disposed within the microspheres by swelling and are not held in place by first characteristic interactions. However, since the nanocrystals are disposed within the microspheres, the microspheres and nanocrystals are the same entity (col. 13, lines 36-60). Furthermore, the microspheres are attached to the substrate through a first characteristic of hydrophobicity (col. 7, lines 38-54). Therefore, Chee et al. do teach the first characteristic interactions between the substrate and the microsphere. Regarding the argument that Chee et al. teach the sealing of pores in order to hold the nanocrystals in place. Chee et al. actually teach the substrate being silica at col. 3, lines 34-36 and later teach the substrate being porous and hydrophobic or hydrophilic for the disposal of microspheres, wherein the microspheres comprise nanocrystals (col. 7, lines 38-54). Furthermore, the disposal through electrostatic forces refers to the first characteristic of microspheres, which are disposed in a porous silica substrate, and wherein the microspheres comprise a second detectable characteristic provided by nanocrystals.

Regarding claim 74-96, Applicant argues that Chee et al. do not disclose, teach or suggest the following limitations of claim 1: "a nanospecies having a first characteristic... a porous material having the first characteristic selected from a hydrophobic characteristic, a hydrophilic characteristic, an electrostatic characteristic; and combinations thereof". However, as cited previously Chee et al. teach a hydrophobic silica (col. 3, lines 34-36) porous material (col. 7, lines 40-54) and having a plurality of pores (col. 3, lines 34-36). Chee et al. refer to microspheres (microspheres are interpreted to be nanospecies) and substrates having the same first hydrophobic, hydrophilic or electrostatic characteristics wherein the microspheres become disposed within the substrate due to the first characteristics (col. 7, lines 38-54). Chee et al. describe the substrate as being hydrophobic or hydrophilic to dispose microspheres within the substrate (col. 7, lines 38-54) and also the substrate being silica (col. 3, lines 34-36). Therefore, the substrate would be hydrophobic silica. Chee et al. disclose the nanocrystals and microspheres being disclosed in the silica (col. 7, lines 38-54; col. 34-37), and the microspheres comprising the optical signature which is a nanocrystal (col. 13, lines 36-60). Therefore, the nanocrystals and microspheres are part of the same structure and collectively comprise the first and second characteristics of being hydrophobic and optically detectable, respectively. Applicant argues that the nanocrystals are disposed within the microspheres by swelling and are not held in place by first characteristic interactions. However, since the nanocrystals are disposed within the microspheres, the microspheres and nanocrystals are the same entity (col. 13, lines 36-60). Furthermore, the microspheres are attached to the substrate through a first characteristic of hydrophobicity (col. 7, lines 38-54). Therefore, Chee et al. do teach the first characteristic interactions between the substrate and the microsphere. Regarding the argument that Chee et al. teach the sealing of pores. Chee et al. actually teaches the substrate being silica at col. 3, lines 34-36 and later teaches the substrate being porous and hydrophobic or hydrophilic for the disposal of microspheres (col. 7, lines 38-54). Furthermore, the disposal through electrostatic forces refers to the first characteristic of microspheres, which are disposed in a porous silica substrate, and wherein the microspheres comprise a second detectable characteristic provided by nanocrystals.

With respect to claims 59-73, Applicant argues that Chee et al. do not disclose, teach or suggest the following limitations of claim 1: "a nanospecies having a first characteristic... a porous material having the first characteristic selected from a hydrophobic characteristic, a hydrophilic characteristic, an electrostatic characteristic, and combinations thereof". However, as cited previously Chee et al. teach a hydrophobic silica (col. 3, lines 34-36) porous material (col. 7, lines 40-54) and having a plurality of pores (col. 3, lines 34-36). Chee et al. refer to microspheres (microspheres are interpreted to be nanospecies) and substrates having the same first hydrophobic, hydrophilic or electrostatic characteristics wherein the microspheres become disposed within the substrate due to the first characteristics (col. 7, lines 38-54). Chee et al. describe the substrate as being hydrophobic or hydrophilic to dispose microspheres within the substrate (col. 7, lines 38-54) and also the substrate being silica (col. 3, lines 34-36). Therefore, the substrate would be hydrophobic silica. Chee et al. disclose the nanocrystals and microspheres being disclosed in the silica (col. 7, lines 38-54; col. 34-37), and the microspheres comprising the optical signature which is a nanocrystal (col. 13, lines 36-60). Therefore, the nanocrystals and microspheres are part of the same structure and collectively comprise the first and second characteristics of being hydrophobic and optically detectable, respectively. Applicant argues that the nanocrystals are disposed within the microspheres by swelling and are not held in place by first characteristic interactions. However, since the nanocrystals are disposed within the microspheres, the microspheres and nanocrystals are the same entity (col. 13, lines 36-60). Furthermore, the microspheres are attached to the substrate through a first characteristic of hydrophobicity (col. 7, lines 38-54). Therefore, Chee et al. do teach the first characteristic interactions between the substrate and the microsphere. Regarding the argument that Chee et al. teach the sealing of pores. Chee et al. actually teaches the substrate being silica at col. 3, lines 34-36 and later teaches the substrate being porous and hydrophobic or hydrophilic for the disposal of microspheres (col. 7, lines 38-54). Furthermore, the disposal through electrostatic forces refers to the first characteristic of microspheres, which are disposed in a porous silica substrate, and wherein the microspheres comprise a second detectable characteristic provided by nanocrystals. Regarding the rejection of claim 7, Examiner recognizes Girot et al. does not have a col. 44, however Girot et al. teach a hydrophobic silica porous material

having a hydrocarbon-derivatized surface at col. 6, line 37-col. 7, line 15. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Chee et al. teach the substrate being silica (col. 3, lines 34-36) and the substrate being hydrophobic (col. 7, lines 38-54). Therefore, the hydrophobic silica material would prevent non-specific binding as taught by Girot et al. (Girot, col. 8, lines 5-11). Furthermore, as discussed above, Chee et al. teach a hydrophobic micropore comprising a semiconductor quantum dot, wherein the micropore is disposed in the hydrophobic substrate. In response to applicant's argument that Girot does not mention the hydrophobic coated semiconductor quantum dot in Chee, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Regarding claims 12-16 and 84-88, Applicant argues that Chee et al. do not disclose, teach or suggest the following limitations of claim 1: "a nanospecies having a first characteristic... a porous material having the first characteristic selected from a hydrophobic characteristic, a hydrophilic characteristic, an electrostatic characteristic, and combinations thereof". However, as cited previously Chee et al. teach a hydrophobic silica (col. 3, lines 34-36) porous material (col. 7, lines 40-54) and having a plurality of pores (col. 3, lines 34-36). Chee et al. refer to microspheres (microspheres are interpreted to be nanospecies) and substrates having the same first hydrophobic, hydrophilic or electrostatic characteristics wherein the microspheres become disposed within the substrate due to the first characteristics (col. 7, lines 38-54). Chee et al. describe the substrate as being hydrophobic or hydrophilic to dispose microspheres within the substrate (col. 7, lines 38-54) and also the substrate being silica (col. 3, lines 34-36). Therefore, the substrate would be hydrophobic silica. Chee et al. disclose the nanocrystals and microspheres being disclosed in the silica (col. 7, lines 38-54; col. 34-37), and the microspheres comprising the optical signature which is a nanocrystal (col. 13, lines 36-60). Therefore, the nanocrystals and microspheres are part of the same structure and collectively comprise the first and second characteristics of being hydrophobic and optically detectable, respectively. Applicant argues that the nanocrystals are disposed within the microspheres by swelling and are not held in place by first characteristic interactions. However, since the nanocrystals are disposed within the microspheres, the microspheres and nanocrystals are the same entity (col. 13, lines 36-60). Furthermore, the microspheres are attached to the substrate through a first characteristic of hydrophobicity (col. 7, lines 38-54). Therefore, Chee et al. do teach the first characteristic interactions between the substrate and the microsphere. Regarding the argument that Chee et al. teach the sealing of pores. Chee et al. actually teaches the substrate being silica at col. 3, lines 34-36 and later teaches the substrate being porous and hydrophobic or hydrophilic for the disposal of microspheres (col. 7, lines 38-54). Furthermore, the disposal through electrostatic forces refers to the first characteristic of microspheres, which are disposed in a porous silica substrate, and wherein the microspheres comprise a second detectable characteristic provided by nanocrystals. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the nanoparticles of Bawendi et al. are not relied upon for the first characteristic, which is provided by Chee et al., but is relied upon for teaching a hydrophobic quantum dot. Bawendi et al. teach a hydrophobic quantum dot, which would have been obvious for use in the porous material of Chee et al. in order to prevent dissociation from a binding surface (Bawendi; col. 2, lines 2-5) and to prevent the degradation of fluorescence (Bawendi; col. 6, line 66-col. 7, line 7). In response to applicant's argument that Bawendi does not mention the hydrophobic coated semiconductor quantum dot in Chee, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

With respect to claims 17 and 89, Applicant argues that Chee et al. do not disclose, teach or suggest the following limitations of claim 1: "a nanospecies having a first characteristic... a porous material having the first characteristic selected from a hydrophobic characteristic, a hydrophilic characteristic, an electrostatic characteristic, and combinations thereof". However, as cited previously Chee et al. teach a hydrophobic silica (col. 3, lines 34-36) porous material (col. 7, lines 40-54) and having a plurality of pores (col. 3, lines 34-36). Chee et al. refer to microspheres (microspheres are interpreted to be nanospecies) and substrates having the same first hydrophobic, hydrophilic or electrostatic characteristics wherein the microspheres become disposed within the substrate due to the first characteristics (col. 7, lines 38-54). Chee et al. describe the substrate as being hydrophobic or hydrophilic to dispose microspheres within the substrate (col. 7, lines 38-54) and also the substrate being silica (col. 3, lines 34-36). Therefore, the substrate would be hydrophobic silica. Chee et al. disclose the nanocrystals and microspheres being disclosed in the silica (col. 7, lines 38-54; col. 34-37), and the microspheres comprising the optical signature which is a nanocrystal (col. 13, lines 36-60). Therefore, the nanocrystals and microspheres are part of the same structure and collectively comprise the first and second characteristics of being hydrophobic and optically detectable, respectively. Applicant argues that the nanocrystals are disposed within the microspheres by swelling and are not held in place by first characteristic interactions. However, since the nanocrystals are disposed within the microspheres, the microspheres and nanocrystals are the same entity (col. 13, lines 36-60). Furthermore, the microspheres are attached to the substrate through a first characteristic of hydrophobicity (col. 7, lines 38-54). Therefore, Chee et al. do teach the first characteristic interactions between the substrate and the microsphere. Regarding the argument that Chee et al. teach the sealing of pores. Chee et al. actually teaches the substrate being silica at col. 3, lines 34-36 and later teaches the substrate being porous and hydrophobic or hydrophilic for the disposal of microspheres (col. 7, lines 38-54). Furthermore, the disposal through electrostatic forces refers to the first characteristic of microspheres, which are disposed in a porous silica substrate, and wherein the microspheres comprise a second detectable characteristic provided by nanocrystals. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941

(Fed. Cir. 1992). In this case, Efros et al. is not relied upon for the teaching of a first characteristic, and it would have been obvious to coat the microsphere of Chee et al. with stearic acid as taught by Efros et al., in order to provide additional stability to the quantum dot by isolating the surface of the active portion of the quantum dot from the effects of the environment (Efros; col. 4, lines 34-37). In response to applicant's argument that Efros does not mention the porous material having a first characteristic that causes the nanospecies having the first characteristic to be disposed in the pores of the porous material in Chee, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

With respect to claims 18 and 90, Applicant argues that Chee et al. do not disclose, teach or suggest the following limitations of claim 1: "a nanospecies having a first characteristic... a porous material having the first characteristic selected from a hydrophobic characteristic, a hydrophilic characteristic, an electrostatic characteristic, and combinations thereof". However, as cited previously Chee et al. teach a hydrophobic silica (col. 3, lines 34-36) porous material (col. 7, lines 40-54) and having a plurality of pores (col. 3, lines 34-36). Chee et al. refer to microspheres (microspheres are interpreted to be nanospecies) and substrates having the same first hydrophobic, hydrophilic or electrostatic characteristics wherein the microspheres become disposed within the substrate due to the first characteristics (col. 7, lines 38-54). Chee et al. describe the substrate as being hydrophobic or hydrophilic to dispose microspheres within the substrate (col. 7, lines 38-54) and also the substrate being silica (col. 3, lines 34-36). Therefore, the substrate would be hydrophobic silica. Chee et al. disclose the nanocrystals and microspheres being disclosed in the silica (col. 7, lines 38-54; col. 34-37), and the microspheres comprising the optical signature which is a nanocrystal (col. 13, lines 36-60). Therefore, the nanocrystals and microspheres are part of the same structure and collectively comprise the first and second characteristics of being hydrophobic and optically detectable, respectively. Applicant argues that the nanocrystals are disposed within the microspheres by swelling and are not held in place by first characteristic interactions. However, since the nanocrystals are disposed within the microspheres, the microspheres and nanocrystals are the same entity (col. 13, lines 36-60). Furthermore, the microspheres are attached to the substrate through a first characteristic of hydrophobicity (col. 7, lines 38-54). Therefore, Chee et al. do teach the first characteristic interactions between the substrate and the microsphere. Regarding the argument that Chee et al. teach the sealing of pores. Chee et al. actually teaches the substrate being silica at col. 3, lines 34-36 and later teaches the substrate being porous and hydrophobic or hydrophilic for the disposal of microspheres (col. 7, lines 38-54). Furthermore, the disposal through electrostatic forces refers to the first characteristic of microspheres, which are disposed in a porous silica substrate, and wherein the microspheres comprise a second detectable characteristic provided by nanocrystals. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Damle et al. is not relied upon for the teaching of a first characteristic, and it would have been obvious to coat the microsphere of Chee et al. with octadecylamine as taught by Damle et al., in order to provide a hydrophobic coating for stability of the nanoparticle (Damle; pg. 1389, right column, first par.; pg. 1391, section Results and discussion, first par.). In response to applicant's argument that Damle does not mention the first characteristic in Chee, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Regarding claims 61-65, In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The 103(a) rejections using the references of Chee in view of Girot and Bawendi, do not include knowledge gleaned only from the applicant's disclosure, and the motivation to combine is disclosed in each of the references, as discussed above. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, each of the combined references provide a motivation to combine elements as discussed above. The motivation to combine the three prior art references of Chee in view of Girot and Bawendi is found in Bawendi, wherein the nanocrystals of Chee in view of Girot, are made with specific hydrophobic compounds as taught by Bawendi, in order to create nanocrystals that are highly luminescent and stable in aqueous solutions, to prevent charge transfer across the region and to maintain the desired isolation between individual quantum dots (Bawendi; col. 6, lines 11-13; col. 7, lines 44-56).

With respect to claim 66, In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The 103(a) rejections using the references of Chee in view of Girot and Efros, do not include knowledge gleaned only from the applicant's disclosure, and the motivation to combine is disclosed in each of the references, as discussed above. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be

established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, each of the combined references provide a motivation to combine elements as discussed above. The motivation to combine the three prior art references of Chee in view of Girot and Efros is found in Efros, wherein the nanocrystals of Chee in view of Girot, are passively coated with stearic acid as taught by Efros, in order to provide additional stability to the quantum dot by isolating the surface of the active portion of the quantum dot from the effects of the environment and prevent the binding substrate from absorbing a majority of the excitation of the fluorescent label (Efros, col. 4, lines 34-37).

Regarding claim 67, In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The 103(a) rejections using the references of Chee in view of Girot and Damle, do not include knowledge gleaned only from the applicant's disclosure, and the motivation to combine is disclosed in each of the references, as discussed above. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, each of the combined references provide a motivation to combine elements as discussed above. The motivation to combine the three prior art references of Chee in view of Girot and Damle is found in Damle, wherein the nanocrystals of Chee in view of Girot, are coated with octadecylamine as taught by Damle et al., in order to provide a hydrophobic coating for stability of the nanoparticle (Damle; pg. 1389, right column, first par.; pg. 1391, section Results and discussion, first par.).